

Time-ordered products for stochastic systems biology

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Short Abstract — The time-ordered product framework of quantum field theory can also be used to understand salient phenomena in stochastic biochemical networks. It can be used to derive Gillespie’s Stochastic Simulation Algorithm, as well as generalizations thereof including particle-based spatial stochastic simulation algorithms.

Keywords — stochastic chemical kinetics; time-ordered product; stochastic simulation; spatial models

I. OUTLINE

THE time-ordered product framework of quantum field theory can also be used to understand salient phenomena in stochastic biochemical networks. It can be used to derive Gillespie’s Stochastic Simulation Algorithm, as well as generalizations thereof that simulate hybrid systems combining stochastic events together with ordinary differential equations. It can be used to derive maximum-likelihood parameter learning algorithms for stochastic chemical kinetics, and to understand the flow of molecules (or other particles) through reaction schemes that contain irreversible transitions, such as reaction schemes occurring in the study of signal transduction. And it can be used to carefully rederive and generalize particle-based spatial stochastic simulation algorithms.

II. A FEW DETAILS

The master equation (chemical or more generally) for a stochastic system may be expressed as $dp/dt = W \cdot p(t)$ where W is the time-evolution operator. This equation has formal solution $\exp(tW) \cdot p(0)$. If W can be decomposed as a sum $W = W_0 + W_1$, then there is a perturbation theory for $\exp(tW)$ in terms of $\exp(tW_0)$ and its perturbations by W_1 . Indeed, the Time-Ordered Product Expansion (TOPE) formula [1] for the solution of a master equation can be expressed as [2]:

$$\exp(tW) \cdot p_0 = \exp(t(W_0 + W_1)) \cdot p_0 \\ = \sum_{k=0}^{\infty} \left[\int_0^t dt_1 \int_{t_1}^t dt_2 \cdots \int_{t_{k-1}}^t dt_k \exp((t-t_k)W_0) W_1 \exp((t_k-t_{k-1})W_0) \cdots W_1 \exp(t_1 W_0) \right] \cdot p_0$$

This formula leads to exact algorithms, unlike (eg) the Trotter Product Formula for the exponential of a sum of matrices.

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Using TOPE, the global time-translation operator W appearing in the master equation can be decomposed into W_0 , consisting of the (negative) diagonal part of all reaction processes and discrete-time events, and W_1 , the off-diagonal part of all discrete-time events. For pure chemical reaction networks this decomposition leads to the Gillespie Stochastic Simulation Algorithm (SSA). Note that the recursive exponential form immediately enables nested perturbations for multiscale modeling. Unlike the Dyson series in quantum field theory which is asymptotic, for these stochastic processes the TOPE converges. This algorithmic interpretation of TOPE has been extended to reacting objects with parameters [3], hybrid reaction/ODE systems [1,3], and parameter-learning algorithms for stochastic chemical kinetics [3,4].

Calculations show the following results relevant to spatial stochastic simulation algorithms. Multimolecular reactions can be reduced to multiple reactions of the form $A+B \leftrightarrow C$. One may break up the time evolution operator into various parts and use TOPE iteratively on them. Thus, decompose $W = W_{\text{diff}} + V_{\text{react}} - D_{\text{react}}$, and $D_{\text{react}} = D_{\text{decay}} + D_{\text{interact}}$ where D_{interact} is for “forward” reactions eg. $A+B \rightarrow C$ and D_{decay} is for “backwards” reactions eg. $C \rightarrow A+B$. All D and V entries are nonnegative. We consider Gaussian interaction kernels (propensity as a function of distance). As a starting point, $W_0 = W_{\text{diff}}$ can be solved exactly using the Heat Kernel. As an inner loop, $W_1 = W_{\text{diff}} - D_{\text{decay}}$ can be also solved exactly since the forward reaction propensity D_{decay} of any extant particle is constant. Next, $W_2 = W_1 - D_{\text{interact}}$ yields a plethora of Gaussian integrals, summable subsets of which correspond to spatial stochastic simulation algorithms.

III. CONCLUSION

Much can be learned about stochastic biochemical models using simplified versions of the tools of QFT.

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